STRUCTURAL STUDIES ON STREPTOTHRICIN

BY

GEORGE BUCKMASTER WHITFIELD, JR.

B. A., Cornell College, 1946
M. S., University of Illinois, 1951

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
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Introduction

Streptothricin is a toxic antibiotic discovered by Waksman and Woodruff in 1942. Since this antibiotic is a potent anti-bacterial agent, it was of general interest to correlate structure with toxicity and anti-bacterial activity with a view toward suggesting structural analogs which might be expected to have activity without the great toxic effects of streptothricin, itself.

Discussion of Results

Streptothricin, on acid hydrolysis, yields carbon dioxide, ammonia, and three ninhydrin-positive components. The three ninhydrin-positive components have been separated on cellulose columns and a study has been made of the physical and chemical properties of Compound C.

Compound C resembles a hexosamine as it gives positive Benedict's and Elson-Morgan tests. Chemical analysis of the amine hydrochloride indicates a molecular weight of 380, $C_{11}H_{23}N_4O_6 \cdot 2HCl$. Periodate studies show Compound C takes up 2 moles at pH 4.5 and 3 moles at pH 8.5, indicating a molecular weight of 275. No carbonyl derivatives of Compound C have been isolated in a crystalline state.

Compound C is degraded by mild alkali treatment to form two new ninhydrin-positive components, with simultaneous loss of carbon dioxide, ammonia, and reducing power.

Streptothricin is also degraded by mild alkali treatment, initially losing a mole of carbon dioxide forming a new ninhydrin-positive component, and finally losing a mole of ammonia forming three ninhydrin-positive components. The chemical properties of the product obtained when streptothricin loses a mole of carbon dioxide were also investigated.

Summary

1. The three ninhydrin-positive components formed by the acid-hydrolysis of streptothricin have been separated

chromatographically and a study has been made of the properties of Compound C.

2. Compound C is a basic substance whose hydrochloride analyzes for $C_{11}H_{23}N_4O_6 \cdot 2HCl$. It reduces Benedict's solution and gives a positive Elson-Morgan test for hexosamines.
3. Compound C forms two ninhydrin-positive components on mild alkali treatment, with the loss of ammonia and carbon dioxide.
4. Streptothricin loses a mole of carbon dioxide forming a single new compound when subjected to mild alkaline hydrolysis, and loses a mole of ammonia forming three ninhydrin-positive components when the treatment is prolonged.
5. Physical and chemical properties have been investigated for the product formed from streptothricin by the loss of a mole of carbon dioxide.

VITA

The author was born on December 4, 1923, in Newark, New Jersey, and attended grammar school in the Chicago Public School System. He graduated from Morgan Park Military Academy, Chicago, in 1940, and entered Cornell College, Mount Vernon, Iowa, the same year. He enlisted in the Army Air Forces in 1942 and served as a Bombardier-Navigator in the Asiatic-Pacific theater. He married the former Joan Lucille Root, in Rockford, Illinois, in 1944. Following separation from the service in February, 1946, he re-entered Cornell College, receiving the B. A. degree in August, 1946. He entered the Graduate College, University of Illinois, in September, 1946. From 1947 to 1951, the author was employed in the Antibiotic Research Department, The Upjohn Company. He re-entered the University of Illinois in 1951, receiving the M. S. degree in 1951. The author has held an Abbott-Lilly-Upjohn fellowship since 1951.